Iran J Cancer Preven. 2015 August; 8(4):e3439. DOI: 10.17795/ijcp.3439

Published online 2015 August 24. **Research Article**

# Recurrence and Five-Year Survival in Colorectal Cancer Patients After Surgery

Seyed Reza Fatemi,[1] Mohamad Amin Pourhoseingholi,[1,*] Farshad Asadi,[1] Mohsen Vahedi,[2] Sara Pasha,[1] Leila Alizadeh,[1] and Mohammad Reza Zali[1]

[1]Gastroenterology and Liver Diseases Research Center, Research Institute for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences, Tehran, IR Iran
[2]Department of Epidemiology and Biostatistics, School of Public Health, Tehran University of Medical Sciences, Tehran, IR Iran

*Corresponding author: Mohamad Amin Pourhoseingholi, Gastroenterology and Liver Diseases Research Center, Research Institute for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences, Tehran, IR Iran. Tel: +98-2122432515, E-mail: aminphg@gmail.com

**Received:** July 6, 2015; **Accepted:** July 11, 2015

**Background:** Colorectal cancer (CRC) is a common malignancyworldwide and its outcome is most closely related to the extent of disease at presentation. Early diagnosis of an asymptomatic recurrence increases the likelihood of a complete surgical resection.
**Objectives:** The aim of this study was to evaluate the incidence of colorectal cancer recurrence and survival rate within 5 years, after surgery.
**Patients and Methods:** During the 9-year period since 21st Mar, 2004 to 20th Mar, 2013, patients whose primary colorectal cancer were resected in Taleghani hospital, Tehran, Iran were selected in a historical cohort. The necessary data such as demographic, age, gender, family history of CRC, site and size of tumor, stage of tumor, operation details, histological results, treatment method, histopathologic, etc. were collected. Then the recurrence and survival of colorectal cancer within 5 years after operation and their risk factors were evaluated. P value less than 0.05 were considered significant. All analysis was done using SPSS software.
**Results:** A total of 107 patients underwent resection for colorectal cancer during the study period, with mean age of 53.50 ± 12.68 years (range 24 - 76 years), survival rate of 73.8% (rectum 70.0% and colon 75.9%), and mean survival time of 142.17 ± 21.60 month. The recurrence rate of CRC patients, during five years after surgery was 5.7%. Regional lymph nodes, Distance metastasis and Adjuvant therapy were significant prognosis factors of survival after surgery.
**Conclusions:** The rate of recurrence in Iranian patients was low, which could be due to improvement of exactness and expertise of surgeons or better adjuvant therapy. The significant association between survival and adjuvant therapy clarifies this finding. Early diagnosis and primary detection could increase the rate of survival.

*Keywords:* Colorectal Cancer; Surgical Resection; Survival; Recurrence

## 1. Background

Colorectal cancer (CRC) is a common cancer worldwide (1). This malignancy is a public health burden in most industrialized countries and a most common cause of cancer-related deaths in the world (2). The incidence and mortality rate of this cancer is increasing in Iran and it is predicted that Iranian population may be experiencing an acceleration of its burden in future (3-5).

A surgical resection is the only curative modality for localized colon cancer. It is the primary treatment modality for CRC, and outcome is most closely related to the extent of disease at presentation. The location of the primary tumor may also have prognostic significance. For each stage, cancers arising at or below the peritoneal reflection (rectosigmoid and rectum) have a worse five-year survival rate than those arising more proximally (6). Furthermore, within the rectum, distal cancers have a worse prognosis than more proximal lesions.

Over the last 50 years, a gradual shift toward right-sided or proximal colon cancers has been observed (5). The survival rates of CRC vary throughout the world due to quality of care, including surgical techniques, which is a predictor of outcomes for local recurrence and cure rates (7, 8). CRC that has metastasized, or spread, to the regional lymph nodes carries a worse prognosis and a higher risk for recurrence. Studies showed that 15 to 30 percent of patients diagnosed with node-negative colorectal cancer experience disease recurrence within 2 - 5 years (9, 10). This high recurrence rate and a higher incidence of colorectal cancer in subjects at high risk of being CRC, highlights a healthcare opportunity for surveillance or interventions to reduce the morbidity associated with CRC (11).

## 2. Objectives

The aim of this study was to evaluate the incidence of colorectal cancer recurrence and survival rate within 5 years, after being affected by this cancer, with considering the effects of other clinical and demographic factors.

## 3. Patients and Methods

This was a historical cohort study in which all patients whose primary colorectal cancer were resected only by the one expert staff of colorectal surgeon or under his supervision and registered in the Taleghani Hospital, Tehran, since 21st Mar, 2004 to 20th Mar, 2013 entered to the study.

The necessary data such as demographic, age, gender, family history of CRC, site and size of tumor, stage of tumor, operation details, histological results, treatment method, etc. had been extracted from medical records. All patients were followed for prognosis, mortality status and recurrence after the surgery (by repeated periodic visits, colonoscopy and telephone contact). Survival time was calculated from the date of surgery registration until death or the end of the study.

Due to protocol of CRC management, for patients with stages II-III and some symptomatic stage IV, a colectomy (surgical removal of the tumor and regional lymph nodes and nearby tissues) were done and then chemotherapy based on 5-fluorouracil was offered to patients younger than 75 years with stage III or IV colon cancer or complicated stage II. Postoperative chemoradiation was offered only to those with stage II or stage III of rectosigmoid cancer when the local clearance was in doubt and preoperative chemoradiation was given to those with fixed T4 lesions.

Chi-square test and Kaplan–Meier analysis have been done to find the prognosis factors, associated to survival and recurrence. P values of less than 0.05 were considered statistically significant. All analysis carried out, using SPSS software, version 17.

## 4. Results

A total of 107 patients (51.2% men) who underwent resection for colorectal cancer during the study period, entered to this study. 23.4% of patients had positive family history of CRC, and 53.8% were sporadic CRC. The mean age was 53.50 ± 12.68 years (range 24 - 76 years), and the survival rate was 73.8% with mean survival time of 142.17 ± 21.60 month. The recurrence rate after surgery was 5.7% and all of them were alive till the end of study. The mean duration of recurrence after surgery was 3.50 ± 1.23 years. Region of recurrences were: five patients (83.3%) near to site of anastomosis or previous tumor and one patient exactly at site of anastomosis. The demographic and clinicopathological factors associated with survival time after surgery were presented in Tables 1 and 2. According to log-rank test, Regional lymph nodes, Distance metastasis and Adjuvant therapy were the prognosis factors of survival in CRC patients after surgery, respectively. Patients with N1 regional LN, M0 level of metastasis and Adjuvant therapy had higher survival. Also, there was no significant association between type of surgery and risk of death in patients under study (Table 3).

The demographic and clinicopathological factors associated with risk of recurrence are presented in Tables 4 and 5. According to the results, none of the demographic and clinicopathological factors was significantly associated with recurrence after surgery.

**Table 1.** Demographic Factors and Five Years Survival After Surgery in Colorectal Cancer Patients

| Variables | No. (%) of Death | Survival Time/Std. Error, Mo | P Value |
|---|---|---|---|
| **Gender** | | | 0.672 |
| Male | 15 (27.3) | 84.20/7.79 | |
| Female | 13 (25.0) | 161.32/20.49 | |
| **Age, y** | | | 0.176 |
| ≤ 50 | 10 (23.2) | 151.29/25.29 | |
| > 50 | 18 (28.1) | 7.98/5.44 | |
| **Family history** | | | 0.555 |
| Negative | 22 (26.8) | 149.42/17.51 | |
| Positive | 6 (24.0) | 84.55/8.47 | |
| **BMI, kg/m²** | | | 0.474 |
| 18.6 - 24.9 | 18 (30.0) | 125.42/25.66 | |
| 25 - 29.9 | 8 (20.5) | 82.65/6.72 | |
| **Category of CRC** | | | 0.646 |
| ≥ 30 | 2 (25.0) | 78.13/13.40 | |
| Sporadic | 12 (26.1) | 62.19/5.13 | |
| HNPCC | 15 (26.3) | 148.14/23.97 | |
| FAP | 1 (33.3) | 29.00/0.00 | |

**Table 2.** Clinicopathological Factors and Five Years Survival After Surgery in Colorectal Cancer Patients

| Variables | No. (%) of Death | Survival Time/Std. Error, Mo | P Value |
|---|---|---|---|
| **Histology** | | | 0.306 |
| Adenocarcinoma | 26 (25.2) | 144.84/22.02 | |
| Others | 2 (50.0) | 41.62/9.19 | |
| **Primary tumor site** | | | 0.289 |
| Rt. colon | 8 (34.8) | 129.43/30.09 | |
| Lt. colon | 20 (24.7) | 88.14/6.41 | |
| **Regional LN** | | | 0.023 |
| N0 | 9 (16.7) | 95.29/7.58 | |
| N1 | 12 (40.0) | 125.19/24.80 | |
| N2 | 6 (40.0) | 59.54/12.50 | |
| **Distant metastasis** | | | < 0.001 |
| Mx | 2 (11.7) | 75.03/5.90 | |
| M0 | 18 (25.3) | 143.78/22.95 | |
| M1 | 8 (66.73) | 36.77/10.77 | |
| **Grade of tumor** | | | 0.215 |
| Well diff | 10 (18.2) | 178.21/19.56 | |
| Moderate diff | 10 (38.5) | 78.49/9.92 | |
| Poor diff | 3 (30.0) | 60.01/17.24 | |
| **Radiotherapy** | | | 0.782 |
| No | 19 (27.19) | 157.19/ 17.10 | |
| Yes | 7 (21.9) | 83.74/ 7.91 | |
| **Neoadjuvant** | | | 0.436 |
| No | 24 (28.6) | 138.31/ 21.79 | |
| Yes | 2 (12.5) | 84.10/10.28 | |
| **Adjuvant therapy** | | | 0.018 |
| No | 11 (36.7) | 58.32/8.47 | |
| Yes | 15 (21.4) | 157.64/24.45 | |

**Table 3.** Type of Surgery and Mortality, After Surgery in Colorectal Cancer Patients

| Type of Surgery | No (%) of Death | P Value |
|---|---|---|
| **Partial colectomy** | 14 (23.0) | 0.643 |
| **Total colectomy** | 3 (37.5) | 0.643 |
| **Other techniques** | 6 (22.2) | 0.643 |

**Table 4.** Demographic Factors and Recurrence After Surgery in Colorectal Cancer Patients

| Variables | No. (%) of Recurrence | P Value |
|---|---|---|
| **Gender** | | 0.357 |
| Male | 4 (7.4) | |
| Female | 2 (3.8) | |
| **Age, y** | | 0.532 |
| ≤ 50 | 2 (4.7) | |
| > 50 | 4 (6.3) | |
| **Family history** | | 0.434 |
| Negative | 4 (4.9) | |
| Positive | 2 (8.0) | |
| **BMI, kg/m²** | | 0.274 |
| 18.6 - 24.9 | 2 (3.4) | |
| 25 - 29.9 | 4 (10.3) | |
| ≥ 30 | 0 (0.0) | |
| **Category of CRC** | | 0.870 |
| Sporadic | 3 (6.7) | |
| HNPCC | 3 (5.3) | |
| FAP | 0 (0.0) | |

**Table 5.** Clinicopathological Factors and Recurrence after Surgery in Colorectal Cancer Patients

| Variables | No (%) of Recurrence | P Value |
|---|---|---|
| **Histology** | | 0.617 |
| Adenocarcinoma | 6 (5.9) | |
| Other histology | 0 (0.0) | |
| **Primary tumor site** | | 0.621 |
| Rt. colon | 1 (4.5) | |
| Lt. colon | 5 (6.2) | |
| **Size of tumor, cm** | | 0.917 |
| < 1 | 0 (0.0) | |
| 1 - 5 | 4 (5.5) | |
| > 5 | 1 (4.2) | |
| **Depth of tumor** | | 0.846 |
| T1 | 0 (0.0) | |
| T2 | 1 (4.0) | |
| T3 | 3 (5.2) | |
| T4 | 0 (0.0) | |
| **Regional LN** | | 0.616 |
| N0 | 3 (5.6) | |
| N1 | 1 (3.4) | |
| N2 | 0 (0.0) | |
| **Distant metastases** | | 0.717 |
| Mx | 1 (5.9) | |
| M0 | 3 (4.3) | |
| M1 | 0 (0.0) | |
| **Grade of tumor** | | 0.326 |
| Well diff | 5 (9.1) | |
| Moderate diff | 0 (0.0) | |
| Poor diff | 0 (0.0) | |
| Undifferentiated | 0 (0.0) | |
| **Radiotherapy** | | 0.509 |
| No | 3 (4.3) | |
| Yes | 2 (6.3) | |
| **Neoadjuvant therapy** | | 0.183 |
| No | 3 (3.6) | |
| Yes | 2 (12.5) | |
| **Adjuvant therapy** | | 0.520 |
| No | 1 (3.3) | |
| Yes | 4 (5.8) | |
| **Type of surgery** | | 0.281 |
| Partial colectomy | 2 (3.7) | |
| Total colectomy | 0 (0.0) | |
| Other techniques | 3 (11.5) | |

## 5. Discussion

This study revealed that, in patients who underwent resection for colorectal cancer, the survival rate is high and the recurrence rate was just 5.7%. The evaluation of post-surgical survival of colorectal cancer is necessary due to comparing results together and then reevaluates cause of differences (kind of surgery, experience of surgeons, doing chemotherapy or chemo radiotherapy and its regimens, quality of post-surgical care and surveillance).

There was no correlation between BMI and CRC survival in this study, which is different from many similar previous researches (12, 13). No age and gender relationship were observed with survival of CRC patients in this study, however some Iranian studies indicated that colorectal cancer occurs at a younger age (14). No patients in recurrence group faced death till the end of study. This statistics is better than other sites in Iran and other countries (15, 16), and similar to some Asian studies (17), which could be due to improvement of exactness and expertise of surgeon or better adjuvant therapy or difference stages in the patients who were operated. The significant association between survival and adjuvant therapy clarifies this finding too. However, the effectiveness of these treatments in the lower stages needs to be evaluated.

The number of examined lymph nodes and Distance metastasis statistically predicted the survival, which is similar to study that indicated the risk of death was higher in patients with distant metastasis (18). Tumor size, grade of tumor and some other clinical factors were not associated to survival, which is in contrast to western studies (19).

The incidence of CRC is lower in Iran compared to Western countries; however, its burden has been increasing in recent years (20, 21). In addition, five year survival rate of CRC has been reported to be lower than the world (22, 23). It seems that among the prognostic factors explored so far, the most important are those that relate to early diagnosis of cancer. So, primary detection is feasible since efficient screening modalities are available (24).

Due to limited data about survival and recurrence of colorectal cancer after surgery and its risk factors in different areas of Iran, our study would be helpful to improving surveillance (pre and post-surgical), survival and recurrence of CRC and at least better managements and control of its risk factors. The evaluation of incidence and duration of colorectal cancer recurrence (where site, stage at time of presentation and site of recurrence) could conduct us to the better planning of post-surgical follow up, reevaluation of kind of surgery, adjuvant and neoadjuvant chemotherapy and chemoradiotherapy, in order to increase the survival of patients.

The limitation of this study is low sample size of patients who underwent resection for colorectal cancer. So in some survival comparison, the results were not significant. It needs to conduct multicenter study in order to merge the patient's dataset and increase reliability of results for future researches in Iran.

## Acknowledgement

Authors appreciate the Research Institute for Gastroenterology and Liver Diseases for supporting this study.

## Authors' Contributions

SRF and MAP conceived and designed this study and interpreted the results and drafted the manuscript. FA, MV and SP participated writing revising the manuscript. LA and SP contributed to data gathering and approved the final manuscript. MRZ supervised the study and approved the draft of manuscript. All authors read and improved the final manuscript.

## Conflict of interest

There is no conflict of interest.

## Financial Disclosure

This study was sponsored by a grant from the Gastroenterology and Liver Disease Research Center, Shahid Beheshti University of Medical Sciences, Tehran, IR Iran.

## References

1. Jemal A, Simard EP, Dorell C, Noone AM, Markowitz LE, Kohler B, et al. Annual Report to the Nation on the Status of Cancer, 1975-2009, featuring the burden and trends in human papillomavirus(HPV)-associated cancers and HPV vaccination coverage levels. *J Natl Cancer Inst.* 2013;**105**(3):175–201.
2. Parkin DM, Ferlay J, Curado MP, Bray F, Edwards B, Shin HR, et al. Fifty years of cancer incidence: CI5 I-IX. *Int J Cancer.* 2010;**127**(12):2918–27.
3. Azadeh S, Moghimi-Dehkordi B, Fatem SR, Pourhoseingholi MA, Ghiasi S, Zali MR. Colorectal cancer in Iran: an epidemiological study. *Asian Pac J Cancer Prev.* 2008;**9**(1):123–6.
4. Pourhoseingholi MA, Vahedi M, Moghimi-Dehkordi B, Pourhoseingholi A, Ghafarnejad F, Maserat E, et al. Burden of hospitalization for gastrointestinal tract cancer patients - Results from a cross-sectional study in Tehran. *Asian Pac J Cancer Prev.* 2009;**10**(1):107–10.
5. Pourhoseingholi MA, Faghihzadeh S, Hajizadeh E, Gatta G, Zali MR, Abadi AR. Trend analysis of gastric cancer and colorectal cancer mortality in Iran, 1995-2003. *Iran J Cancer Prev.* 2011;**4**(1):38–43.
6. Halvorsen TB, Johannesen E. DNA ploidy, tumour site, and prognosis in colorectal cancer. A flow cytometric study of paraffin-embedded tissue. *Scand J Gastroenterol.* 1990;**25**(2):141–8.
7. Rabeneck L, Davila JA, El-Serag HB. Is there a true "shift" to the right colon in the incidence of colorectal cancer? *Am J Gastroenterol.* 2003;**98**(6):1400–9.
8. Huang L, Li TJ, Zhang JW, Liu S, Fu BS, Liu W. Neoadjuvant chemotherapy followed by surgery versus surgery alone for colorectal cancer: meta-analysis of randomized controlled trials. *Medicine (Baltimore).* 2014;**93**(28):e231.
9. Krarup PM, Nordholm-Carstensen A, Jorgensen LN, Harling H. Anastomotic leak increases distant recurrence and long-term mortality after curative resection for colonic cancer: a nationwide cohort study. *Ann Surg.* 2014;**259**(5):930–8.
10. Wong CKH, Law WL, Wan YF, Poon JTC, Lam CLK. Health-related quality of life and risk of colorectal cancer recurrence and All-cause death among advanced stages of colorectal cancer 1-year after diagnosis. *BMC cancer.* 2014;**14**(1):337.
11. Stoian M, State N, Rusu E, Stoica V, Gavril RS, Gherasim A, et al. Malignancy and mortality of colorectal polyps. *Rev Med Chir Soc Med Nat Iasi.* 2014;**118**(2):399–406.
12. Murphy TK, Calle EE, Rodriguez C, Kahn HS, Thun MJ. Body mass index and colon cancer mortality in a large prospective study. *Am J Epidemiol.* 2000;**152**(9):847–54.

13. Terry P, Giovannucci E, Bergkvist L, Holmberg L, Wolk A. Body weight and colorectal cancer risk in a cohort of Swedish women: relation varies by age and cancer site. *Br J Cancer.* 2001;**85**(3):346–9.
14. Aryaie M, Roshandel G, Semnani S, Asadi-Lari M, Aarabi M, Vakili MA, et al. Predictors of Colorectal Cancer Survival in Golestan, Iran: A Population-based Study. *Epidemiol Health.* 2013;**35**.
15. Edge SB, Byrd DR, Compton CC. *AJCC (American Joint Committee on Cancer) Cancer Staging Manual.* 7th ed. New York: Springer; 2010.
16. Sanei B, Mahmoudieh M, Kolahdouzan M, Mehrabi Koushki A, Ferasat F. Survival Time and Recurrent Rate in Patients with Rectum Cancer. *J Isfahan Med Sch.* 2013;**31**:1194–207.
17. Law WL, Chu KW. Anterior Resection for Rectal Cancer With Mesorectal Excision. *Ann Surg.* 2004;**240**(2):260–8.
18. Al-Ahwal MS, Shafik YH, Al-Ahwal HM. First national survival data for colorectal cancer among Saudis between 1994 and 2004: what's next? *BMC Public Health.* 2013;**13**:73.
19. Aguero F, Murta-Nascimento C, Gallen M, Andreu-Garcia M, Pera M, Hernandez C, et al. Colorectal cancer survival: results from a hospital-based cancer registry. *Rev Esp Enferm Dig.* 2012;**104**(11):572–7.
20. Pourhoseingholi MA, Zali MR. Colorectal cancer screening: Time for action in Iran. *World J Gastrointest Oncol.* 2012;**4**(4):82–3.
21. Pourhoseingholi MA, Fazeli Z, Ashtari S, Bavand-Pour FS. Mortality trends of gastrointestinal cancers in Iranian population. *Gastroenterol Hepatol Bed Bench.* 2013;**6**(Suppl 1):S52–7.
22. Moradi A, Khayamzadeh M, Guya M, Mirzaei HR, Salmanian R, Rakhsha A, et al. Survival of colorectal cancer in Iran. *Asian Pac J Cancer Prev.* 2009;**10**(4):583–6.
23. Esna-Ashari F, Sohrabi MR, Abadi AR, Mehrabian AA, Mofid B, Bohluli M, et al. Colorectal Cancer Prevalence According to Survival Data in Iran-2007. *Iran J Cancer Prev.* 2009;**2**:15–8.
24. Moghimi-Dehkordi B, Safaee A. An overview of colorectal cancer survival rates and prognosis in Asia. *World J Gastrointest Oncol.* 2012;**4**(4):71–5.